

*FIRST AMENDMENT AND RESPONSE TO OFFICE ACTION*

*U.S. Serial No.: 10/009,292*

*Filed: November 13, 2001*

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**REMARKS**

Claims 1-22 are pending in the present application, which is directed to methods for detecting the effect of test conditions on eukaryotic cells. The present invention may be used, for example, to screen agents for their effect on eukaryotic cells and thereby identify potential anticancer drugs for use in humans and animals. The present invention may also be used in toxicology assays to help determine the toxicity of an agent in humans and animals. Claim 23 has been cancelled and Claims 1, 2, 4-5, 7-8, 13-16, 19 and 21 are currently amended. Claims 1-22 are pending. Favorable consideration of the currently pending claims is respectfully requested in light of these amendments and the following remarks.

**Rejection Under 35 U.S.C. § 112, second paragraph**

The Examiner rejected Claim 1 as being indefinite stating that the metes and bounds of the term “particular” could not be determined. Applicants have amended the claim to recite “test conditions.” Applicants respectfully submit that support for the amendment can be found on at least page 6, lines 26-37, of the specification wherein test conditions are described as including chemical, biological and biochemical agents as well as temperature, pH, pressure, irradiation and other environmental factors.

The Examiner rejected claim 23 for failing to point out that which is included or excluded by the claim language. Applicants have canceled the claim, and accordingly, the rejection is rendered moot.

The Examiner also rejected claim 21 stating that the metes and bounds of the term “effecting” could not be determined. As suggested by the Examiner, Applicants have amended the claim to remove the objectionable term and replace it with the term “performing.”

Applicants accordingly request review and withdrawal of these rejections.

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Rejections Under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-23 under 35 U.S.C. § 103(a) as being unpatentable over Squirrell (U.S. Patent No. 5,648,232) in view of Webster's Dictionary (1984). More specifically, the Examiner stated that U.S. Patent No. 5,648,232 (hereinafter the '232 patent) discloses a method for detecting the presence and/or amount of microorganisms by estimating the amount of adenylate kinase. The Examiner also rejected claims 1-23 under 35 U.S.C. § 103(a) as being unpatentable over Squirrell (U.S. Patent No. 5,798,214) in view of Webster's Dictionary (1984). More specifically, the Examiner stated that U.S. Patent No. 5,798,214 (hereinafter the '214 patent) discloses a method for detecting the presence and/or amount of microorganisms by estimating the amount of adenylate kinase in a sample. The Examiner further stated that neither the '232 patent nor the '214 patent disclose the use of eukaryotic cells, but that Webster's dictionary definition of "microorganism" encompasses the eukaryotic cells in the sample of the present invention. Applicants respectfully traverse the rejection.

The claimed invention is directed to an assay for determining the effect of test conditions on the integrity of eukaryotic cells. In other words, the present claimed invention is directed to monitoring the impairment of eukaryotic cells upon subjecting them to test conditions. The claimed methods can be used to determine the degree of eukaryotic cell lysis caused by the test condition and to determine whether the eukaryotic cells subjected to the test conditions are growing and dividing normally. These particular embodiments are described on at least page 6, lines 16-37 and page 8, lines 11-37, respectively, of the present application.

Test conditions are described at least on page 6, lines 26-37, and include chemical, biological and biochemical agents as well as temperature, pH, pressure, irradiation and other environmental factors. The effect of the test condition is determined by adding ADP to the eukaryotic cell sample subjected to the test condition, detecting ATP in the sample and correlating the ATP detected to the presence of adenlyate kinase. The cells may or may not be lysed prior to the addition of ADP. The presence of

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adenylate kinase indicates the test condition's effect on the integrity of the eukaryotic cell.

The present invention may be used, for example, to screen agents for their effect on eukaryotic cells and thereby identify potential anticancer drugs for use in humans and animals. In one embodiment, a suspected chemotherapeutic agent is added to the eukaryotic cells followed by the addition of ADP to the cells. An increase in ATP content in the sample, as compared to an untreated sample, indicates that the chemotherapeutic agent lysed the cells and is a good drug candidate. At present, assays for detecting the effects of test agents on eukaryotic cells require microscopic examination of the slide containing the cells to determine whether any cell lysis as a result of apoptosis, for example, has occurred. These prior art methods are time consuming and labor intensive. As noted in the specification, alternative methods do exist, but are not ideal. Such alternative methods include measuring the release of radioactive tracers such as Cr\*, which must be first introduced into the cell. These alternative prior art methods are again time consuming and dangerous due the required use of radioactive materials. The methods of the present invention are an important advancement over these prior art methods.

In contrast to the present invention, the '232 and '214 patents merely describe a method for detecting the presence and/or amount of microorganisms in a sample by lysing the microorganisms with, for example, detergent or mechanical means and detecting the amount of ATP in the sample after adding ADP thereto. The '214 patent includes the additional step of binding any adenylate kinase present in the sample to a binding agent prior to the addition of ADP. There is no teaching or suggestion anywhere in either the '232 or the '214 patent that the assays described therein could be used for any other purpose than detecting the presence or amount of a microorganism in a sample. More importantly, there is no teaching or suggestion that the methods described in the '232 and '214 patents could be used to determine the cell integrity of a eukaryotic cell subjected to test conditions.

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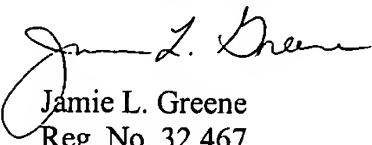
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Applicants respectfully submit that determining the effect of test conditions on eukaryotic cell integrity is very different from detecting the presence and/or amount of a microorganism in a sample. The assay claimed in the present application is in the field of biochemical and pharmaceutical research and diagnosis whereas the assay disclosed in the '232 and '214 patents is for the detection of harmful bacteria in the very different field of food and water safety. Therefore, one would not be motivated to look to the '232 patent or the '214 patent to find a solution to the problems commonly associated with biochemical and pharmaceutical research on eukaryotic cells. Accordingly, Applicants request that the Examiner review and withdraw the rejection.

Conclusion

Based upon the amendments and remarks provided above, Applicants believe that Claims 1-22 are in condition for allowance. A Notice of Allowance is therefore respectfully solicited. If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 745-2473 is respectfully solicited.

Respectfully submitted,



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